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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,056	06/22/2001	Kenneth Kornman	MSA-023.01	6975

25181 7590 04/25/2003

FOLEY HOAG, LLP
PATENT GROUP, WORLD TRADE CENTER WEST
155 SEAPORT BLVD
BOSTON, MA 02110

EXAMINER
CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/888,056	Kornman
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 21, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above, claim(s) *28-37* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-27* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 1
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I and the appropriate species in paper submitted on March 21, 2003, is acknowledged. The traversal is on the ground(s) that there is no burden to search and examine the claims of Groups II and III along with Group I . This is not found persuasive because as mentioned and made clear in the restriction requirement that examination of Group I along with Groups II and III would require not only the search of 2183 patents in class 436, subclass 501 of Group I but also the search of 4435 patents in class 435, subclass 240.2 belonging to Group II, and 1867 patents in class 536, subclass 22.1 belonging to Group III . This is prima facie burden of search, which has not been rebutted.

Moreover, the applicant argues regarding species election that all the species should be examined because the species of the claims are not necessarily mutually exclusive. No evidence has been presented in support of this argument. On the other hand, the applicant did not address the issue of the patentable distinctiveness of all the species. In absence of the addressing of this issue and proof against the patentable distinctiveness of all the species, the argument to withdraw the election of species requirement is not persuasive.

The requirement is still deemed proper and is therefore made FINAL.

Double Patenting

2. Claims 1, 2, 4, 6, 16, 17, 19, 21, and 22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 48-57 of U.S. Patent No. 6,268,142 B1 (July 31, 2001). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 48-57 of U.S. Patent No. 6,268,142 B1 disclose the instant method for identifying a substance that is likely to prevent or diminish a specific biological response in a subject having an inflammatory disease-associated genotype (inherently present in the alleles disclosed in claim 48), the method comprising the steps of:

a) genotyping at least one subject to identify a test subject, wherein the test subject is a subject having an inflammatory disease-associated genotype;

b) observing in cells obtained from the test subject, or cells propagated therefrom, at least one biomarker (IL-1 protein bioreactivity in this case);

c) contacting the cells obtained from the test subject, or cells propagated therefrom, with a test substance;

d) observing again in the cells obtained from the test subject, or cells propagated therefrom, the at least one biomarker;

wherein a change in the at least one biomarker from an inflammatory disease-associated phenotype to a non-inflammatory disease-associated phenotype identifies a test substance that is likely to prevent or diminish the specific immune response in a subject having the inflammatory disease-associated phenotype.

Claims 48-57 of U.S. Patent No. 6,268,142 B1 also disclose the chromosomal region IL-1RN, and allele 1 of IL-1A(+4845), and biomarker selected from IL-1alpha production.

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CAR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CAR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CAR 3.73(b).

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

5. Claims 1-8 and 16-27 are rejected under 35 U.S.C. 102(e) as being anticipated by Duff et al. (U.S. Patent No. 6,268,142 B1 (July 31, 2001).

Duff et al. teaches method for identifying a substance that is likely to prevent or diminish a specific biological response in a subject having an inflammatory disease-associated genotype (Example 5), the method comprising the steps of:

a) genotyping at least one subject to identify a test subject, wherein the test subject is a subject having an inflammatory disease-associated genotype (Example 1);

b) observing in cells obtained from the test subject, or cells propagated therefrom, at least one biomarker (IL-1 protein bioreactivity in this case) (Examples 2 and 3);

c) contacting the cells obtained from the test subject, or cells propagated therefrom, with a test substance (Column 29, lines 43-60);

d) observing again in the cells obtained from the test subject, or cells propagated therefrom, the at least one biomarker (Column 29, line 61 to Column 30, line 36);

wherein a change in the at least one biomarker from an inflammatory disease-associated phenotype to a non-inflammatory disease-associated phenotype identifies a test substance that is

likely to prevent or diminish the specific immune response in a subject having the inflammatory disease-associated phenotype (Column 29, line 43 to Column 30, line 36 and claim 48).

Duff et al. also disclose the chromosomal region IL-1RN, and allele 1 of IL-1A(+4845), and biomarker selected from IL-1alpha production (claims 48-57).

Duff et al. also teaches inflammatory disease-associated allele from the IL-1 44112332 haplotype (Examples 4, 5, 7, and 8).

Duff et al. also teaches inflammatory disease-associated genotype is associated with a predisposition to coronary artery disease (Example 7).

Duff et al. teaches a method, wherein at least one biomarker is selected from blood or urine IL-1alpha levels (Examples 1, 4, and 5).

Duff et al. teaches a method, wherein the cells are obtained from immune cells and immortalized cell line (Column 34, line 17 to line 61).

Duff et al. teaches a method, further comprising administering an inducer to the cells, known to activate IL-1 production in monocytes or macrophages, prior to or concomitant with each step of observing the one or more biomarkers (promoter as cited by Duff can be considered as an inducer) (Column 34, lines 17-22, and Column 33, line 62 to Column 34, line 3, and Examples 3-8).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 9-10 are rejected under 35 U.S.C. 103(a) over Duff et al. (U.S. Patent No. 6,268,142 B1 (July 31, 2001) in view of Girten et al. (U.S. Patent 5,760,001) (June 2, 1998).

Duff et al teaches the method of claims 1-8, and 16-27 as described above.

Duff et al does not teach a method, wherein the inducer comprises exercise sufficient to cause exercise induced stress.

Girten et al. teach a method, wherein the inducer comprises exercise sufficient to cause exercise induced stress (Column 7, lines 20 to 53).

Duff et al does not teach a method, wherein the exercise is a treadmill stress test.

Girten et al. teach a method, wherein the exercise is a treadmill stress test (Example XIII, Column 18, lines 33-45).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine a method, wherein the inducer comprises

exercise sufficient to cause exercise induced stress of Girten et al. in the method of Duff et al, since Girten et al. states "Thus the present invention provides a method of restraining pathologically elevated cytokine activity in a subject (Abstract, lines 7-9)". Further motivation is provided by Duff et al as Duff et al. states, "Methods and kits for determining whether a subject has or is predisposed to developing a disease which is associated with IL-1 polymorphisms and assays for identifying thepeutics for treating and/or preventing the development of these diseases are provided (Abstract)". An ordinary practitioner would have been motivated to substitute and combine a method, wherein the inducer comprises exercise sufficient to cause exercise induced stress of Girten et al. in the method of Duff et al. in order to achieve the express advantages, as noted by Girten et al., of an invention that provides a method of restraining pathologically elevated cytokine activity in a subject, and also to achieve the express advantages, as noted by Duff et al., of an invention which provide methods and kits for determining whether a subject has or is predisposed to developing a disease which is associated with IL-1 polymorphisms and assays for identifying theapeutics for treating and/or preventing the development of these diseases.

8. Claims 11-15 are rejected under 35 U.S.C. 103(a) over Duff et al. (U.S. Patent No. 6,268,142 B1 (July 31, 2001) in view of Hallahan et al. (U.S. Patent 5,962,424) (October 5, 1999).

Duff et al teaches the method of claims 1-8, and 16-27 as described above.

Duff et al does not teach a method, wherein the inducer comprises a subcutaneous injection of an irritant monosodium urate crystals.

Hallahan et al. teach a method, wherein the inducer comprises a subcutaneous injection of an irritant monosodium urate crystals (Example XVII, Column 43, line 64 to column 44, line12, and Example XVI, Column 40, lines 58-63).

Duff et al does not teach a method, wherein the at least one biomarker includes the dimensions and/or duration of skin erythrema resulting from the subcutaneous injection.

Hallahan et al. teach a method, wherein the at least one biomarker includes the dimensions and/or duration of skin erythrema resulting from the subcutaneous injection. (Example XVII).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine a method, wherein the inducer comprises a subcutaneous injection of an irritant monosodium urate crystals of Hallahan et al. in the method of Duff et al, since Hallahan et al. states "The compositions and methods described are suitable for use in the delivery of selected agents to tumor vasculature, as may be used in the diagnosis and therapy of solid tumors (Abstract, last sentence)". Further motivation is provided by Duff et al as Duff et al. states, "Methods and kits for determining whether a subject has or is predisposed to developing a disease which is associated with IL-1 polymorphisms and assays for identifying thepeutics for treating and/or preventing the development of these diseases are provided (Abstract)". An ordinary practitioner would have been motivated to substitute and combine a method, wherein the inducer comprises a subcutaneous injection of an irritant monosodium urate crystals of Hallahan et al. in the method of Duff et al, in order to achieve the express advantages, as noted by Hallahan et al., of an invention that provides compositions and methods suitable for

use in the delivery of selected agents to tumor vasculature, as may be used in the diagnosis and therapy of solid tumors and also to achieve the express advantages, as noted by Duff et al., of an invention which provide methods and kits for determining whether a subject has or is predisposed to developing a disease which is associated with IL-1 polymorphisms and assays for identifying thepeutics for treating and/or preventing the development of these diseases.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph. D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703)746-4979.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti

ARUN K. CHAKRABARTI
PATENT EXAMINER

Arun Chakrabarti,

Patent Examiner,

April 15, 2003